Prion Protein Phylogeny Correlates with Species Barriers to Spongiform Disease

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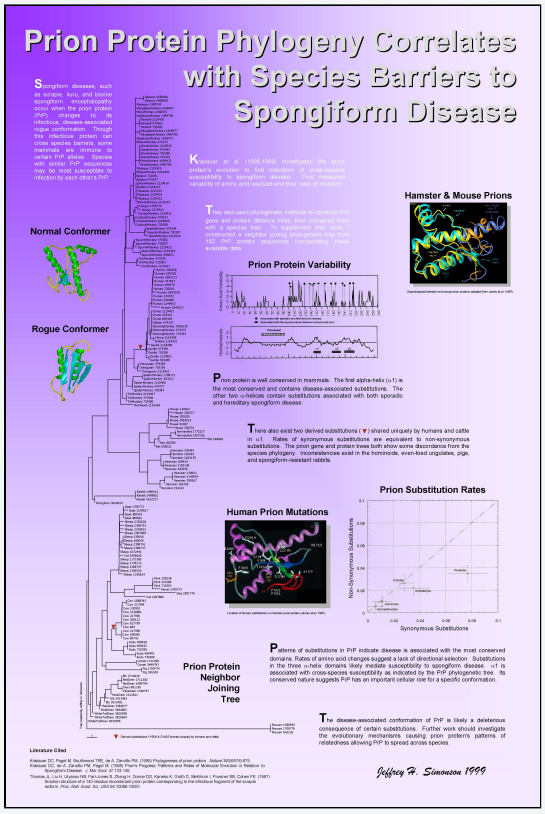

Spongiform diseases occur when the prion protein (PrP) changes to its infectious, disease-associated conformation. This infectious protein can cross species barriers. Species with similar PrP sequences may be most susceptible to infection by each other's PrP. Krakauer et al. (1996,1998) investigated the prion protein's evolution to find indicators of cross-species susceptibility to spongiform disease. They measured variability of amino acid residues and their rates of mutation. They also used phylogenetic methods to construct PrP gene and protein distance trees and compared them with a species tree. Prion protein is well conserved in mammals. The first alpha-helix (a1) is the most conserved and contains disease-associated substitutions. The other two a-helices contain substitutions associated with both sporadic and hereditary spongiform disease. Rates of synonymous substitutions are equivalent to non-synonymous substitutions. The prion gene and protein trees both show some discordance from the species phylogeny. Patterns of substitutions in PrP indicate disease is associated with the most conserved domains; rates of amino acid changes suggest a lack of directional selection. Substitutions in the three alpha-helix domains likely mediate susceptibility to spongiform disease. a1 is associated with cross-species susceptibility. Its conserved nature suggests PrP has an important cellular role for a specific conformation.

Literature Cited

Krakauer DC, Pagel M, Southwood TRE, de A. Zanotto PM. (1998) Phylogenesis of prion protein. Nature 380(6576):675.

Krakauer DC, de A. Zanotto PM, Pagel M. (1998) Prion's Progress: Patterns and Rates of Molecular Evolution in Relation to Spongiform Disease. J. Mol. Evol. 47:133-145.